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A ONE-DAY PRESEASONAL TREATMENT IN POLLEN ALLERGY: PROPOSED TES--ETC(U)
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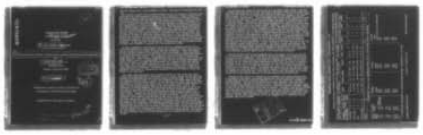

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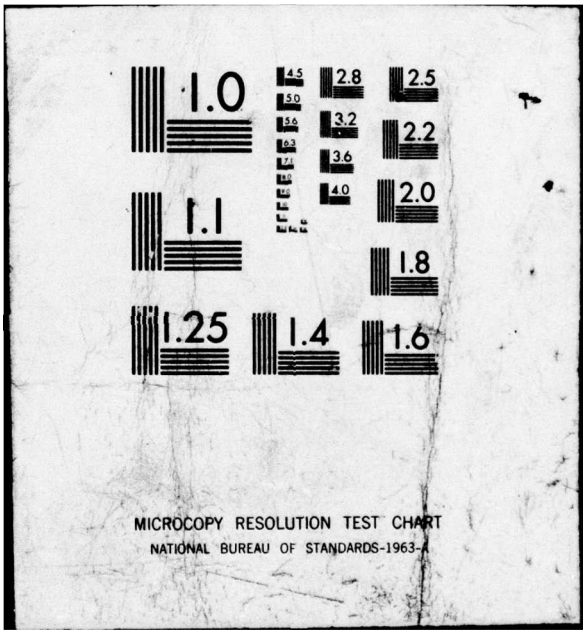
1.0
1.1
1.25
1.4
1.6
1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0
4.5
5.0
5.6
6.3
MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

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(12)

OFFICE OF NAVAL RESEARCH

(15) Contract N00014-76-C-0228 NEW

NR 202-078

(9) FINAL TECHNICAL REPORT, 0001AD

(6) A one-day preseasonal treatment in pollen allergy: proposed testing and injection procedures.

by

(10) Mary H. Loveless, M. D.

22 Cavalry Road,

Westport, Connecticut 06880

(11) 30 Sep[redacted]976

(12) 4p.

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Loveless (Mary H.) 392197
Westport, Conn.

A ONE-DAY PRESEASONAL TREATMENT IN POLLEN ALLERGY: Proposed Testing and Injection Procedures.

Mary H. Loveless, M.D., Contract N00014-76-C-0228. Final Report due September 30, 1976.

The plan was to analyze data accumulated during the past two decades on 93 persons with pollen hay fever whose preseasonal therapy had been completed in a single session of several hours by means of repeated intracutaneous injections given at 10-minute intervals. The amounts of antigen had been highly individualized, the aim being to convey as much as could be tolerated in each injection. For the starting dose, tolerance was guaged, not only by the patient's description of past seasonal symptoms, but particularly by his current susceptibility to ocular instillations of allergen which uncovered his requirement for a minimal allergic reaction in the conjunctiva. (The relation between this requirement and an allergic patient's tolerance toward inhaled or injected antigen had been explored in earlier studies.) Once therapy had been inaugurated, the local response and any focal signs that were generated served to determine the size of the next dose. This tailoring of treatment to individual tolerance gave rise to a wide assortment of dosage patterns and to numerous adverse developments (fortunately, of mild and fleeting nature). Despite these obstacles, the time-saving quality and the typical efficacy of the once yearly treatment prompted a search through the 188 records for clues to suitable, pre-planned schedules. It was hoped that the availability of testing and injection procedures would encourage other allergists to appraise the 1-day immunization method.

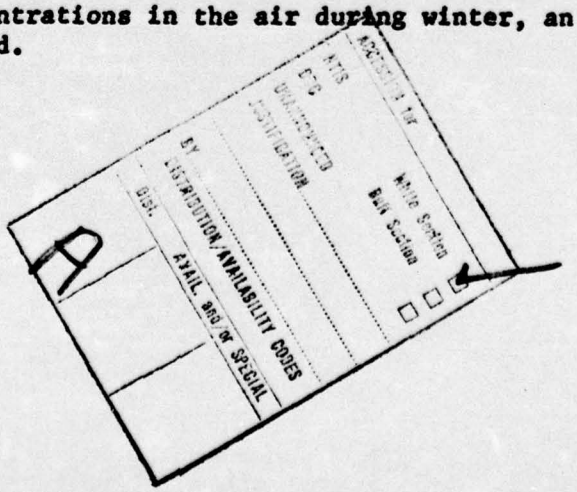
Pertinent information surrounding each of the 188 1-day treatments given the 93 patients was transferred to single sheets, showing the succession of doses, the total dose, and the intensity of any untoward reactions that were encountered. After these sheets had been arranged according to the associated ocular requirement, a cursory examination of the doses and adverse results made it clear that the 11 different requirements could be consolidated into 4 eye classes. This promised to simplify the task of constructing dosage schedules. Before setting up comprehensive tables for analysis of each of the four ocular classes, however, it seemed prudent to reduce the risk of untoward developments by lowering the amount of allergen that had promoted focal responses in any past session. The courses, after this slight modification, were then examined in such a way that the first dose given each member of the group was listed in a column so that a range and a median value could be determined. The second and subsequent injections, as well as the cumulative total amount of allergen given (expressed in terms of protein N units), were handled in the same manner.

After these ranges and median values had been computed for each of the four ocular classes (which were symbolized by the letters, A, B, C and D), inquiry was made into the increment of allergen that had been involved between successive doses. It was found that the increment amounted roughly to 12½ per cent according to the median figures and that this applied to all four ocular classes. At the same time, the actual sizes of the doses (especially as reflected in the median values for the ocular group) had been smallest in Class A and had become gradually larger as the class shifted to B, C, and D. This combination of findings suggested that preliminary dosage schedules might be set up for each class on the basis of the median figures for the first, second and subsequent injections; also that a uniform 12½ per cent incremental schedule could be used for all 1-day courses. Indeed, once the median first dose had been injected without focal sequelae, one could follow the 12½ per cent schedule of increases. In short, the ocular requirement of the patient would determine at what point on this uniform schedule his therapy would commence and, according to the median total dose taken by the ocular class, at what point it could be ended. Adaptations of this scheme could be made for persons who had exhibited past intolerance to the median starting dose of the eye class: the allotment being selected at a lower level but still within the group range. And for those who had tolerated this median first dose in earlier treatments but whose clinical result had proven less than optimal, the starting amount could be elevated by one or two steps on the 12½ per cent schedule so as to increase the total dose for the current session. This approach was put to practical test in 51 pollen allergics who were scheduled for one-day therapy in 1976.

In preparation for trials with the 12½ per cent incremental dosage scheme, a plan for successive injections was set up (see lower half of the table) after the calculated allotments had been rounded out to amounts that could be measured in a routine 1- or 2-ml tuberculin syringe. All but a few of the 51 participants in the 1976 experiments had taken earlier one-day immunizations. After determining their current ocular requirements, most of them started this year's therapy with the median value found for the appropriate class in the past survey. The amount of allergen actually employed is expressed in terms of a range and a median value for the first injection, which will be seen in the table to have been larger as the ocular class shifted upward. Similarly, the cumulative total dose for the session was greater for successive ocular classes. The number of injections, however, was similar, ranging from 9 to 12. Although 18 of these 489 divided doses generated untoward manifestations, only 2 stemmed from the initial injection, thereby vindicating the usefulness of the eye test as a clue to tolerance toward the allotted first dose. Of the remaining incidents, 8 were apparently invited by an inadvertent or an overoptimistic skipping of an allotment prescribed by the 12½ per cent schedule. Eliminating these from consideration, the overall incidence of focal reactions associated with the schedule amounted to 20 per cent, as compared to one of 29 per cent uncovered by the survey of past empirical one-day immunizations. It will be noted in the table that none of the 1976 developments exceeded slight-plus in severity. Few failed to abate spontaneously when more than the routine 10-minute interval was allowed before therapy was continued. Recalculation of the median first dose after lowering the amounts given in the two provocative injections of 1976 should improve the incidence of tolerance next year, especially if the remaining injections adhere strictly to the 12½ per cent increments.

Because occasional patients and allergists hold a bias against the idea of using the eye for sensitivity tests, scratch-testing of the skin was added to the regimen in 1976 to evaluate it as a substitute. When the paired results were inspected, the minimal requirement for the scratch reaction was found to be somewhat greater than for the ocular procedure and the difference carried significance at the 95 per cent level of confidence according to the t test. When paired end-points that had been procured for 54 pollen-allergics in 1961 and 114 in 1960 were subjected to t test, the scratch requirement was again found to be somewhat higher. The overall impression given was that one could crudely estimate the ocular end-point by halving the strength of allergen required for a minimal response in the scratch test. Thus those who lack eye-test data might still be able to make use of the proposed schedules for one-day immunization described above.

Although further studies are indicated by the experiments with single-session therapy discussed in this report, encouraging progress has been made toward the original goal of developing testing and injection procedures for a one-day prophylactic treatment in inhalant allergy. The eye-test has given clues to what comprises a safe first dose, and a schedule for additional injections has been constructed after analyzing past, empirical, one-day sessions which were tailored solely to individual tolerance and which suggested that 12½ per cent incremental doses might be feasible. Although it was hoped to include mold-spore allergy in the year's studies, too few cases were available for meaningful results. However, the principle of single session immunization should be applicable, especially for patients whose symptoms are limited to the summer season of maximal spore production. For the lower concentrations in the air during winter, an additional one-day treatment might well be needed.



Mary H. Locke

EXPERIMENTAL ONE-DAY TREATMENTS GIVEN 51 POLLEN ALLERGICS in 1976

using the eye-test to estimate the first dose of allergen, and 12½% increments[γ] in the ensuing injections

Minimal ocular requirement just before 1st injection			1st endermal dose (in PN units)		Total dose involved (in PN units)		No. of injections involved		No. of adverse incidents arising			
Strength of allergen (PN units/ml)	Ocular class	Number of patients	Range	Median	Range	Median	Range	Median	Slight-minus	Slight	Slight-plus	Total number
10 to 60	A	6	2½ to 25	10	43 to 318	193	7 to 14	9	2	2	0	4
80 to 240	B	26	5 to 37½	25	70 to 1200	390	2 to 14	9-10	5	1	2	8
320	C	6	10 to 100	37½	538 to 1525	1,000	8 to 17	11-12	3	0	0	3
640 or more	D	13	25 to 150	100	338 to 4075	1,975	5 to 14	10	2	1	0	3
Total		51							12	4	2	18

γ SCHEDULE OF 12½ per cent INCREMENTAL DOSES used in 1976 One-Day Serial Injections

Calculated doses	Rounded doses[#]	Rounded doses	Rounded doses	Rounded doses
5.0	5.0 (.05ml of	15.0	40.0	125(0.125 ml of 1,000 U/ml)
5.6	5.0 .100 U/ml)	15.0	47.5	125
6.3	5.0	17.5	52.5	150
7.1	7.5	20.0	60.0	175
8.0	7.5	22.5	67.5	200
9.0	10.0	25.0	75.0	225
10.4	10.0	30.0	85.0	250
11.4	12.5	32.5	95.0	275
12.8	12.5	37.5	100.0	300

[#] to facilitate measurement in tuberculin-type syringe, preferably of 2 ml size.